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| EXAMINER INITIAL | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | l | DATE F PRIATE | |
| (mm | 4,636,492 | 1/13/87 | Kettner et al. | 514 | 18 | | | |
| | 4,644,055 | 2/17/87 | Kettner et al. | 530 | 330 | RE | CEIVE | |
| | 4,652,552 | 3/24/87 | Kettner et al. | 514 | 18 | 1 . | | |
| | 4,808,523 | 2/28/89 | Revel et al. | 435 | 69.51 | JUL | 3 1 2002 | |
| | 5,104,853 | 4/14/92 | Beason et al. | 514 | 12 | | | |
| | 5,225,354 | 7/6/93 | Knowles et al. | 436 | 548 | LOTTUE | NTER 1600/29 | |
| .] / | 5,304,481 | 4/19/94 | Davies et al. | 435 | 196 | | | |
| | 5,756,465 | 5/26/98 | Sleath et al. | 514 | 17 | | | |
| • | | FOREIGN F | PATENT DOCUM | ENTS | | | | |
| EXAMINER | | | | | 01/1001 400 | TRANS | LATION | |
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| | 0 272 671 | 6/24/88 | EP | | | | | |
| | 0 533 350 | 3/24/93 | EP | | | | | |
| am | WO91/15577 | 10/17/91 | WIPO | | | | | |
| em | WO93/05071 | 3/18/93 | WIPO | | | | | |
| | OTHER DOCUMEN | NTS (Includin | ia Author, Title, Da | ate. Pertinen | t Pages, Etc.) | | | |
| EXAMINER NITIAL | | | | | | | r de la companya de l | |
| | Beuscher et al. IL-1 beta is secreted by activated murine macrophages as biologically inactive precursor. <i>J. Immunol.</i> 144 , 2179 (1990). | | | | | | | |
| | Black et al. Generation of biologically active interleukin-1β by proteolytic cleavage of the inactive precursor. <i>J. Biol. Chem.</i> 263 , 9437 (1988). | | | | | | | |
| | Black et al. A pre-aspartate-specific protease from human leukocytes that cleaves pro-interleukin 1β. J. Biol. Chem. 264 , 5323 (1989). | | | | | | kin 1β. <i>J</i> . | |
| | Black et al. Activation of i | nterleukin-1 | by a co-induced | protease. FE | BS Letts. 247, 3 | 386 (1989). | | |
| 1 | Black et al. Identification of Cytokines. (J. Oppenher | of a protease | that processes in | terleukin-1β. | In Molecular a | nd Cellular | Biology | |

DATE CONSIDERED 4-16-03 EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

EXAMINER

| FORM PTO-1 | 1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY. DOCKET NO. VPI/SW/002 CIP2 FWC DIV2 CON | SERIAL NO. 09/670,106 | | | |
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| | | FILING DATE September 26, 2000 | GROUP 1614 | | | |
| | | | | | | |
| - VE | OTHER DOCUMENTS (Including Author, Title | e, Date, Pertinent Pages, Etc.) | | | | |
| EXAMINER INITIAL | | | | | | |
| am | Black et al. Purification and molecular cloning of the 15G , CH 201 (1991). | IL-1β processing enzyme. J. (| Cell. Biochem. Supp | | | |
| cm~ | Black et al. The proteolytic activation of Interleukin-1 Therapy. (N. Ackerman , R. Bonney, A. Welton, Eds | lb. In <i>Progress in Inflammation</i>) pp. 85–89 Birkhauser Verlag | Research and J. Basel (1990). | | | |
| <u>ain</u> | CAPLUS DN 116 50949, Rosenthal et al. J. Clin. Inv | | | | | |
| <u>un</u> | CAPLUS DN 118: 208112, Thornberry et al. Nature | | | | | |
| um | Casano et al. The structure and complete nucleotide interleukin-1β converting enzyme (ICE). Genomics 2 | | encoding | | | |
| <u>. </u> | Cerretti et al. Molecular cloning of the IL-1β process | ing enzyme. J. Cell. Biol. Supp | . F15, P506 (1991). | | | |
| | Cerretti et al. Molecular cloning of the IL-1β processing enzyme. Cytokine p. 137 (1991). Cheremisinoff et al. (eds). Biotechnology Applications and Research, Technomics Publishing Co, pp. 21, 541-557 (1985). | | | | | |
| | | | | | | |
| | Dower et al. The interleukin-1 system: Receptors, lig | | | | | |
| | Dreyer et al. Inhibition of human immunodeficiency virus 1 protease in vitro: rational design analogue inhibitors. <i>Proc. Natl. Acad. Sci. USA</i> 86 , 9752 (1989). | | | | | |
| | Hazuda et al. The kinetics of interleukin 1 secretion from activated monocytes. <i>J. Biol. Chem.</i> 263 8473 (1988). Howard et al. IL-1-converting enzyme requires aspartic acid residues for processing of the IL-1β precursor at two distinct sites and does not cleave 31-kDa IL-1a. <i>J. Immunol.</i> 147, 2964 (1991). | | | | | |
| | | | | | | |
| | Kitada et al. New peptide models for studying racemization. Chem. Pharm. Bull. 26, 585 (1978). | | | | | |
| | Knittel et al. Stimulation of insulin secretion from pancreatic islets by the cholecystokinin-tetrapeptide analogs Trp-Pro-Asp-Phe-NH ₂ and Trp-Pro-Asp-Phe(4'-NO ₂)-NH ₂ . Pept. Res. 3 , 224 (1990). | | | | | |
| | Koga et al. Comparative study on specifics of rat cat substrate binding sites are involved in their specificities. | id differences as 0). | | | | |
| | Kostura et al. Identification of a monocyte specific pr Acad. Sci. USA 86, 5227 (1989). | e-interleukin 1β convertase ac | livity. <i>Proc. Natl.</i> | | | |
| | Lee et al. Generation of cDNA probes directed by an Science 239, 1288 (1988). | nino acid sequence: Cloning of | urate oxidase. | | | |
| 4 | Malek et al. Amino acid sequence of an invertebrate Biochem. Biophys. Res. Comm. 126, 195 (1985). | FBP aldolase (from Drosophila | melanogaster). RECEI | | | |

JUL 3 1 2002

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

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| JUL 2 6 2002 | | APPLICANT P. Sleath et al. | CONFIRMATION NO, 5809 GROUP 1614 | | | |
| | | FILING DATE September 26, 2000 | | | | |
| E. | | | | | | |
| & TRA | OTHER DOCUMENTS (Including Author, Title | , Date, Pertinent Pages, Etc.) | | | | |
| EXAMINER INITIAL | | | (A) | | | |
| Um | March et al. Cloning, sequence and expression of two distinct human interleukin-1 complementary DNAs. <i>Nature</i> 315, 641 (1985). | | | | | |
| | McQuade et al. A synthetic HIV-1 protease inhibitor vimaturation. Science 247, 454 (1990). | | | | | |
| | Mosley et al. Determination of the minimum polypeptide lengths of the functionally active sites of human interleukins 1 alpha and 1 beta. <i>Proc. Natl. Acad. Sci. USA</i> 84, 4572 (1987). | | | | | |
| | Rasnick. Synthesis of peptide fluoromethyl ketones and the inhibition of human cathepsin B. <i>Anal. Biochem.</i> 149 , 461 (1985). | | | | | |
| | Sigma catalog. pp. 294-295, 312, 351-352 (1989). | | | | | |
| | Sleath, P. et al. Substrate specificity of the protease that processes human interleukin-1β. <i>J. Biol. Chem.</i> 285 , 14526 (1990). | | | | | |
| | Smith et al. Visualization of time-dependent inactivation of human tumor cathepsin B isoenzymes by a peptidyl fluoromethyl ketone using a fluorescent print technique. <i>Anticancer Res.</i> 8 , 525 (1988). | | | | | |
| | Stein. Catalysis by human leukocyte elastase 4. Role of secondary subsite interactions. <i>J. Am. Chem. Soc.</i> 107 , 5767 (1985). | | | | | |
| | Suggs, S. et al. Use of synthetic oligonucleotides as hybridization probes: Isolation of cloned cDNA sequences for human β2-microglobulin. <i>Proc. Natl. Acad. Sci. USA</i> 78, 6613 (1981). | | | | | |
| | Tomasselli et al. Substrate analogue inhibition of active site titration of purified recombinant HIV-1 protease. <i>Biochemistry</i> 29 , 264 (1990). | | | | | |
| | Van Noorden et al. Cysteine proteinase activity in arthritic rat knee joints and the effects of a selective systemic inhibitor, Z-Phe-Ala-CH₂F. <i>J. Rheumatol.</i> 15 , 10 (1988). | | | | | |
| | Woessner. Matrix metalloproteinases and their inhibitors in connective tissue remodeling. FASEB J. 5, 2145 (1991). | | | | | |
| | Young et al. Human interleukin 1 beta is not secreted transfected cDNA. <i>J. Cell. Biol.</i> 107 , 447 (1988). | from hamster fibroblasts cons | stitutively from a | | | |
| | | on with antibody probes. Scien | | | | |

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JUL 3 1 2002

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.